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Scientists reveal how malaria parasites outwit our immune systems

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Malaria parasites are able to disguise themselves to avoid our immune systems, according to research led by Oxford University

researchers based in Kenya and published in the journal *Proceedings of the*

National Academy of Sciences USA (PNAS).

The research team, from the Kenya Medical Research Institute (KEMRI)-Wellcome Trust Programme in Kilifi, Kenya, and the Wellcome Trust Sanger Institute in Cambridge, has shown that the parasites adapt a particular set of molecules they produce, depending on which antibodies they encounter in the human host. This allows the parasites to outwit the immune system.

systems.

Malaria parasites, carried by mosquito bites, are able to disguise

themselves to avoid our immune

' The malaria parasite is very complex, so our immune system mounts many different responses, some more effective than others and many not effective at all,' explains Dr Peter Bull of the Centre for Tropical Medicine at the University of Oxford and the KEMRI-Wellcome Trust Programme, who led the research.

' We know that our bodies have great difficulty in completely clearing infections, which begs the question: how does the parasite manage to outwit our immune response? We have shown that, as children begin to develop antibodies to parasites, the malaria parasite changes its tactics to adapt to our defences.'

Malaria is responsible for over a million deaths every year, mainly in children and pregnant women in Africa and South-east Asia. It is caused by the malaria parasite, which is injected into

Further information

PNAS

<u>Health</u>

- Centre for Tropical Medicine
- The Kenya Medical Research Institute
- The Wellcome Trust



the bloodstream from the salivary glands of infected mosquitoes. There are a number of different species of parasite, but the deadliest is the *Plasmodium falciparum* parasite, which accounts for 90 per cent of deaths from malaria.

The malaria parasite infects healthy red blood cells, where it reproduces. The *P. falciparum* parasite generates a family of molecules, known as PfEMP1, that are inserted into the surface of the infected red blood cells. The cells become sticky

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Dr Peter Bull

and adhere to the walls of blood vessels in tissues such as the brain. This prevents the cells being flushed through the spleen, where the parasites would be destroyed by the body's immune system, but also restricts blood supply to vital organs.

Symptoms can differ greatly between young and older children depending on previous exposure to the parasite. In young children, the disease can be extremely serious and potentially fatal if untreated; older children and adults who have grown up in endemic areas are resistant to severe malaria but rarely develop the ability to rid their bodies of the parasite.

The Wellcome Trust-funded researchers studied malaria parasites in blood samples from 217 Kenyan children with malaria. They found that a group of genes coding for a particular class of PfEMP1 molecule called Cys-2 tended to be switched on when the children had a low immunity to the parasite. As immunity develops, the parasite switches on a different set of genes, effectively disguising it so that immune system cannot clear the infection.

Dr George Warimwe and colleagues at the KEMRI-Wellcome Trust Programme also found an independent association between activity in Cys-2 genes and severe malaria in the children, suggesting that specific forms of the molecule may be more likely to trigger specific disease symptoms.

The findings could suggest a new approach to tackling malaria, in terms of both vaccine development and drug interventions, suggests Dr Bull.

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